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1: Arzneimittelforschung 1989 Oct;39(10):1251-3

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Radiosynthesis of [^{14}C]acarbose.

Maul W, Muller L, Pfitzner J, Rauenbusch E, Schutt H.

Pharma Research Center, Bayer AG, Wuppertal, Fed. Rep. of Germany.

Acarbose (O-4,6-dideoxy-4-[[[(1S, 4R, 5S, 6S)-4,5,6-trihydroxy-3-(hydroxymethyl)-2-cyclohexen-1-yl]amino]- α -D-glucopyranosyl-(1----4)-O- α -D-glucopyranosyl-(1----4)-4-glucopyranose, Bay g 5421), an α -glucosidase inhibitor from Actinoplanes, has been developed for the treatment of diabetes mellitus. To investigate the pharmacokinetics and the biotransformation, ^{14}C -labelled acarbose ([^{14}C]Bay g 5421) was required. About 37 GBq (1 Ci) D-[U- ^{14}C]glucose was used as a precursor to obtain [^{14}C]acarbose with a radiochemical yield of between 1.58 and 2.56%. For fermentation purposes resting cells of the Actinoplanes mutant SN 1667/47 were used under cometabolism conditions with a 10-fold excess of maltose. The specific radioactivities achieved in individual preparations were 7.77 MBq/mg (210 microCi/mg), 8.03 MBq/mg (217 microCi/mg), and 9.14 MBq/mg (247 microCi/mg), with a radiochemical purity of greater than 98% in each case. By hydrolysis and subsequent investigation of the hydrolysis products it was shown that [^{14}C]carbon atoms originating from the radioactive glucose are present only in the core and not in the maltose unit of [^{14}C]acarbose.

PMID: 2610716 [PubMed - indexed for MEDLINE]

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L3 ANSWER 39 OF 39 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1981:204413 CAPLUS

DOCUMENT NUMBER: 94:204413

TITLE: **Acarbose** (BAY g 5421) and homologous
.alpha.-glucosidase inhibitors from Actinoplanaceae

AUTHOR(S): Mueller, L.; Junge, B.; Frommer, W.; Schmidt, D.;
Truscheit, E.

CORPORATE SOURCE: Inst. Biochem., Bayer A.-G., Wuppertal, D-5600, Fed.
Rep. Ger.

SOURCE: Enzyme Inhibitors, Proc. Meet. (1980), 109-22.
Editor(s): Brodbeck, Urs. Verlag Chem.: Weinheim,
Fed. Rep. Ger.
CODEN: 45FGAU

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Inhibitors of .alpha.-glucosidases effective against pancreatic
.alpha.-amylase and intestinal enzymes such as glucoamylase, sucrase, and
maltase were discovered in culture broths of Actinoplanaceae. These
inhibitors are oligosaccharides in which an unsatd. cyclitol unit bound to
4,6-dideoxy-4-amino-D-glucopyranose is the integral part in a chain of
1,4-.alpha.-linked D-glucopyranose units. These form a series of
homologous compds. with a different no. of glucose units in the mol.
Inhibitory activity is strongly dependent on mol. wt. The max. specific
inhibitory activity against sucrase in vitro was attributed to
acarbose (I), which contains 2 glucose units, whereas the
strongest .alpha.-amylase inhibitors were of higher mol. wt. In vivo, I
not only delays the digestion of sucrose, but is also a very potent
inhibitor of starch degrdn. Due to retarded carbohydrate digestion, the
postprandial increment of blood glucose and serum insulin in animals and
man is dose-dependently reduced by I in loading tests with starch or
sucrose. A reduced gain in body wt. in genetically obese Zucker rats fed
carbohydrates and I is due to a dose-dependent redn. of food consumption.

=>

L3 ANSWER 33 OF 39 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:130895 CAPLUS
DOCUMENT NUMBER: 110:130895
TITLE: Alpha-glucosidase inhibitors
AUTHOR(S): Odaka, Hiroyuki; Matsuo, Takao
CORPORATE SOURCE: Cent. Res. Div., Takeda Chem. Ind., Ltd., Osaka, 532,
Japan
SOURCE: Nippon Nogei Kagaku Kaishi (1989), 63(2), 217-19
CODEN: NNKKAA; ISSN: 0002-1407
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review, with 14 refs., on .alpha.-glucosidase inhibition by
acarbose, obtained from Actinoplanes strain SE 50 incubation
medium, and AO-128, obtained from the incubation medium of
Streptomyces hygrosopicus subsp. limoneus. Anti-obesity and
antidiabetes mellitus activities of AO-128 are briefly discussed.

L3 ANSWER 28 OF 39 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 9
ACCESSION NUMBER: 1994:476969 CAPLUS
DOCUMENT NUMBER: 121:76969
TITLE: Comparative study of the action of microbial
inhibitors on various .alpha.-glucosidases
AUTHOR(S): Akulova, N. Yu.; Kazanina, G. A.; Selezneva, A. A.
CORPORATE SOURCE: State Res. Technol. Inst. Antibiot. Enzymes Med.
Applicat., St. Petersburg, Russia
SOURCE: Prikladnaya Biokhimiya i Mikrobiologiya (1994), 30(1),
83-7
CODEN: PBMIAK; ISSN: 0555-1099
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB The action of a new .alpha.-glucosidase inhibitor from
Streptomyces sp. and **Acarbose** on .alpha.-glucosidases of
various origins has been studied. Differences in specificity, efficiency,
nature and type of inhibition of microbial glucosidases and some enzymes
of the small intestine mucosa by the biol. active substances studied were
revealed. It is suggested that the inhibitor from **Streptomyces**
sp. (in combination with a diet) can be used for regulation of some
disturbances in carbohydrate metab.

L3 ANSWER 22 OF 39 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:667748 CAPLUS

DOCUMENT NUMBER: 127:318162

TITLE: Manufacture of the acarviosyl transferase of Actinoplanes by expression of the cloned gene for preparation of **acarbose** and **acarbose** homologs

INVENTOR(S): Crueger, Anneliese; Dellweg, Hans-Georg; Lenz, Juergen Georg; Schroeder, Werner; Pape, Hermann; Goeke, Klaus; Schaper, Beate; Hemker, Michael; Piepersberg, Wolfgang; Distler, Juergen; Stratmann, Ansgar

PATENT ASSIGNEE(S): Bayer A.-G., Germany

SOURCE: Eur. Pat. Appl., 37 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 796915	A2	19970924	EP 1997-104115	19970312
EP 796915	A3	19990414		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
DE 19625269	A1	19970925	DE 1996-19625269	19960625
US 5989882	A	19991123	US 1997-816105	19970314
AU 9716361	A1	19970925	AU 1997-16361	19970317
JP 09252789	A2	19970930	JP 1997-82458	19970317
CA 2200421	AA	19970922	CA 1997-2200421	19970319
ZA 9702424	A	19970925	ZA 1997-2424	19970320
NO 9701326	A	19970923	NO 1997-1326	19970321
CN 1172161	A	19980204	CN 1997-104903	19970321
BR 9701418	A	19980818	BR 1997-1418	19970321

PRIORITY APPLN. INFO.:

DE 1996-19611252 A 19960322

DE 1996-19625269 A 19960625

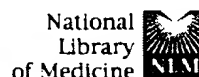
AB The acarviosyl transferase of Actinoplanes SE 50/110 is manufd. by expression of the acbD gene encoding it in a suitable expression host. The enzyme catalyzes exchange of the glycosyl moiety of the glycoside with a free sugar and can be used for converting **acarbose** derivs. into **acarbose** or **acarbose** homologs for use in the treatment of diabetes. The enzyme synthesized by Actinoplanes SE 50/110 is secreted into the culture medium from where it can be rapidly purified. The enzyme has a mol. wt. of 76,000, a pH optimum of 6.2-6.9, a temp. optimum of 30.degree. and is active in the range 20-40.degree., and requires calcium. The enzyme uses a wide range of carbohydrates as acceptors (Markush given). Cloning of the acbD gene for the enzyme is also described. The gene was overexpressed in **Streptomyces lividans** using the vector pUWL199-derived plasmid pAS9.

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PASCAL' ENTERED AT 14:21:02 ON 21 MAY 2003

L1	2 S ACARBOSE AND GLAUCESCENS
L2	70 S ACARBOSE AND STREPTOMYCES
L3	39 DUP REM L2 (31 DUPLICATES REMOVED)



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Field: Author, Limits: Publication Date from 1984 to 1984


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☐ 1: [Crameri R, Hintermann G, Hutter R, Kieser T.](#)

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 Tyrosinase activity in *Streptomyces glaucescens* is controlled by three chromosomal loci.

Can J Microbiol. 1984 Aug;30(8):1058-67.

PMID: 6437655 [PubMed - indexed for MEDLINE]

☐ 2: [Hopwood DA, Hintermann G, Kieser T, Wright HM.](#)

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 Integrated DNA sequences in three streptomycetes form related autonomous plasmids after transfer to *Streptomyces lividans*.

Plasmid. 1984 Jan;11(1):1-16.

PMID: 6369354 [PubMed - indexed for MEDLINE]

☐ 3: [Hintermann G, Crameri R, Vogtli M, Hutter R.](#)

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 Streptomycin-sensitivity in *Streptomyces glaucescens* is due to deletions comprising the structural gene coding for a specific phosphotransferase.

Mol Gen Genet. 1984;196(3):513-20.

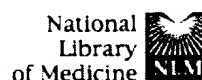
PMID: 6094980 [PubMed - indexed for MEDLINE]

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1: Nature 1987 Feb 26-Mar 4;325(6107):818-21

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Homology between Streptomyces genes coding for synthesis of different polyketides used to clone antibiotic biosynthetic genes.

Malpartida F, Hallam SE, Kieser HM, Motamedi H, Hutchinson CR, Butler MJ, Sugden DA, Warren M, McKillop C, Bailey CR, et al.

Many important antibiotics such as tetracyclines, erythromycin, adriamycin, monensin, rifamycin and avermectins are polyketides. In their biosynthesis, multifunctional synthases catalyse iterated condensation of thio-esters derived from acetate, propionate or butyrate to yield aliphatic chains of varying length and carrying different alkyl substituents. Subsequent modifications, including aromatic or macrolide ring closure or specific methylations or glycosylations, generate further chemical diversity. It has been suggested that, if different polyketide synthases had a common evolutionary origin, cloned DNA coding for one synthase might be used as a hybridization probe for the isolation of others. We show here that this is indeed possible. Study of a range of such synthase genes and their products should help to elucidate what determines the choice and order of condensation of different residues in polyketide assembly, and might yield, by in vitro recombination or mutagenesis, synthase genes capable of producing novel antibiotics. Moreover, because genes for entire antibiotic pathways are usually clustered in Streptomyces, cloned polyketide synthase genes are valuable in giving access to groups of linked biosynthetic genes.

PMID: 3029594 [PubMed - indexed for MEDLINE]

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